UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/693,558	10/20/2000	Elfi Biedermann	25846-0003	7777

25213 7590 06/28/2006

HELLER EHRMAN LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CA 94025-3506

EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 06/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/693,558	BIEDERMANN ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-36 and 55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-36, 55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicants' Response filed February 3, 2006 is acknowledged. Claims 32-36 and 55 remain under consideration wherein nicotinic acid and nicotinamide are the species under consideration in a method for reducing side effects or neutralizing the side effects of a cancerostatic or immunosuppressive agent.

A new Abstract is noted.

A list of co-pending and related applications, regardless of the stage of prosecution, for any of the ten named inventors that relate to the present method of use, is further noted.

Claims 32-36 and 55 were rejected under 35 U.S.C. 112, second paragraph, in the last Office Action as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention with respect to the recitation "or a prodrug thereof" in claims 32, 33, 35, 36 and 55.

In response Applicants provide general textbook information and state, as an example, that the compound may be an ester.

The Examiner is well acquainted with textbook definitions of prodrugs and the general utility of them. However, in the present claims, which define Applicants' invention, for those prodrugs contemplated, as compounds having vitamin PP activity for use in methods for reducing side effects of a cancerostatic or immunosuppressive agent, the metes and bounds of the term "prodrug" cannot be precisely determined. Applicants may consider an amendment to claim 32, wherein those esters considered by Applicants to be prodrugs are recited in the claim.

The rejection of record under 35 U.S.C. 112, second paragraph, is maintained.

In the last Office Action claims 32-36 and 55 were rejected under 35 U.S.C. 102(b) as being anticipated by Nurmukhembetov et al., Kardiologia (abstract). It was asserted Nurmukhembetov teaches the administration of the compound having PP vitamin activity, nicotinamide, to reduce side effects relating to cardiac contractility as a result of an injection of the cancerostatic agent adriblastin.

Applicants argue Nurmukhembetov discloses the pretreatment of nicotinamide prior to injection of adriblastin for the prevention of cardiac contractility. In Applicants' view preventing cardiac contractility disorders, a well-documented side effect of adriamycin, does not anticipate the claimed method for reducing side effects of a cancerostatic agent.

Applicants' argument is not found persuasive and this rejection of record under 35 U.S.C. 102(b) is maintained. In Nurmukhembetov's animal model the administration of 20 mg/kg of nicotinamide 3 days prior to adriamycin administration resulted in an improvement of cardiac parameters. A copy of the Warning that is part of the package insert provided by the manufacturer Pharmacia & Upjohn is provided to show myocardial toxicity is a side effect of adriamycin administration.

Claims 32-36 and 55 were rejected under 35 U.S.C. 102(b) in the last Office Action as being anticipated by Giri et al., Advances in experimental medicine and Biology. A complete copy of the reference is presently provided. It was asserted Giri teaches the administration of the compound having PP vitamin activity, niacin, to reduce the chemically-induced side effect interstitial pulmonary fibrosis that results from administration of the cancerostatic agent bleomycin.

Applicants argue Giri teaches the administration of a combination of products including taurine, and thus Giri does not teach the claimed method for reducing side effects of a cancerostatic agent.

Applicants' argument is not persuasive and this rejection of record under 35 U.S.C. 102(b) is maintained. Bleomycin-induced pneumotoxicity that eventuates in fibrosis is a well-documented side effect. See page 330, lines 18-26. In the animal model set forth by Giri, niacin (nicotinic acid) alone, or in combination with taurine, is beneficially administered to prevent this pulmonary fibrosis. Further, Giri et al. refer to an earlier one of their publications entitled "Niacin attenuates bleomycin-induced lung fibrosis in the hamster," Journal Biochem. Toxicol. (1990). (The reference is presently unavailable to the Examiner.)

Claims 32-36 and 55 were rejected under 35 U.S.C. 102(b) in the last Office Action as being anticipated by Stevens et al., British Journal of Dermatology. A complete copy of the reference is presently provided. It was asserted Stevens teaches the administration of the compound having PP vitamin activity, nicotinic acid, to neutralize a dermatologic side effect, a rash, that was exacerbated by administration of the cancerostatic agent 5-fluorouracil. Pellagra is presented as a chemically-induced side effect secondary to 5-fluorouracil.

Applicants argue "the typical changes of pellagra ... rash and an associated acute deterioration in cerebral function were exacerbated by treatment with 5-fluoruracil" and that nicotinic acid deficiency in patients with malignant disease should be

considered. Applicants urge Stevens does not teach the claimed method for reducing side effects of a cancerostatic agent.

Applicants' argument is not persuasive and this rejection of record under 35 U.S.C. 102(b) is maintained. Stevens' teaching is entitled "Pellagra secondary to 5-fluorouracil." The first line of the Abstract is: The development of pellagra in a patient treated with 5-fluorouracil for malignant disease is reported. One skilled in the oncology art would conclude from such language that the occurrence of pellagra is subordinate to, or occurs immediately after, the administration of the cancerostatic agent. Stevens additionally teaches the exacerbation of the rash and associated acute deterioration in cerebral function with 5-fluorouracil treatment. In either case treatment with nicotinic acid lead to a rapid resolution and gradual improvement of the manifestations of pellagra. See page 579, second column, lines 34-36.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this Final Action is set to expire THREE MONTHS from the mailing date of this Action. In the event a first reply is filed within TWO MONTHS of the mailing date of this Final Action and the Advisory Action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the Advisory Action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the Advisory Action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this Final Action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached from 10:30 to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ardin Marschel, can be reached 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phyllis Spivack

June 24, 2006

Phyllis Spivack
PHYLLIS SPIVACK
PRIMARY EXAMINER